Ser. No. 09/890,371 PATENTS

Atty. Docket No. VOS-020 (107070.129US1)

Amendment in Response to Office Action Dated July 26, 2006

Amendments to the Claims:

The following listing of claims will replace all prior versions, and listings, of claims in the application.

1-53. Canceled.

54. (Previously presented) A method for administering a pharmaceutical composition to a patient in need thereof, comprising:

transnasally administering to the patient a pharmaceutical composition, the pharmaceutical composition comprising:

an active ingredient; and

a carrier comprising a penetrant suspended or dispersed in a solvent,

the penetrant comprising a minute fluid droplet surrounded by a coating of at least one layer of at least two substances, the substances differing by at least a factor of 10 in solubility in a liquid medium,

the substances forming homoaggregates of one substance and/or heteroaggregates of the at least two substances, the average diameter of homoaggregates of the more soluble substance or the average diameter of the heteroaggregates of the at least two substances being smaller than the average diameter of homoaggregates of the less soluble substance, and/or

the more soluble substance solubilizing the droplet and the content of the more soluble substance is up to 99 mol-% of the concentration required to solubilize the droplet or corresponds to up to 99 mol-% of the saturating concentration in an unsolubilized droplet, whichever is higher, and/or

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wherein the elastic deformation energy of the droplet surrounded by the coating is at least five times lower than the deformation energy of red blood cells or of a phospholipid bilayer having fluid aliphatic chains.

- 55. (Previously presented) The method of claim 54, wherein the at least two substances are two forms of a substance.
- 56. (Previously presented) The method of claim 54, wherein the active ingredient is an allergen.
- 57. (Previously presented) The method of claim 54, wherein the active ingredient is an antigen.
- 58. (Currently amended) The method of claim 54, further comprising a compound that is a cytokine or a compound that induces cytokine or anti-cytokine activity.
- 59. (Previously presented) The method of claim 58 wherein the cytokine is IL-4, IL-3, IL-2, TGF, IL-6, TNF, IL-1α, IL-1β, a type I interferon, IFN-alpha, IFN-β, IL-12, IFN-gamma, TNF-β, IL-5 or IL-10.
- 60. (Previously presented) The method of claim 58 wherein the compound with anti-cytokine activity is an anti-cytokine antibody or active fragment, derivative, or analog thereof.
- 61. (Currently amended) The method of claim 58 wherein the <u>compound that is a cytokine or induces cytokine or anti-cytokine activity and the active ingredient are associated with the penetrant.</u>
- 62. (Previously presented) The method of claim 54, wherein the less soluble substance is a lipid, and the more soluble substance is a surfactant.
- 63. (Previously presented) The method of claim 54, wherein the less soluble substance is a lipid, and the more soluble substance is a more soluble form of the lipid.
- 64. (Currently amended) The method of claim 54, wherein the more soluble substance is an agent to be transported across a <u>mucosal</u> barrier, the agent forming common large structures with the less soluble component(s) of the penetrant.

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- 65. (Previously presented) The method of claim 54, wherein the more soluble substance solubilizes the penetrating droplet and is present in concentration not exceeding 99 mol% of the concentration required to disintegrate the droplet or not exceeding 99 mol% of the saturating concentration in the unsolubilized droplet, whichever is higher.
- 66. (Previously presented) The method of claim 54, wherein the less soluble substance is a polar lipid and the more soluble substance is a surfactant or a surfactant-like molecule.
- 67. (Previously presented) The method of claim 54, wherein the less soluble substance is a polar lipid and the more soluble substance is a polar lipid.
- 68. (Previously presented) The method of claim 54, wherein the average diameter of the penetrant is between 25 nm and 500 nm.
- 69. (Previously presented) The method of claim 54, wherein the average diameter of the penetrant is between 30 nm and 250 nm.
- 70. (Previously presented) The method of claim 54, wherein the average diameter of the penetrant is between 35 nm and 200 nm.
- 71. (Previously presented) The method of claim 54, wherein the average diameter of the penetrant is between 40 nm and 150 nm.
- 72. (Previously presented) The method of claim 54, wherein the concentration of penetrant is 0.001 to 20 weight-% of total dry mass in the pharmaceutical composition.
- 73. (Previously presented) The method of claim 54, wherein the concentration of penetrant is between 0.01 w-% and 15 w-% of total dry mass in the pharmaceutical composition.
- 74. (Previously presented) The method of claim 54, wherein the concentration of penetrant is between 0.1 w-% and 12.5 w-% of total dry mass in the pharmaceutical composition.
- 75. (Previously presented) The method of claim 54, wherein the concentration of penetrant is between 0.5 w-% and 10 w-%.of total dry mass in the pharmaceutical composition.

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76. (Previously presented) The method of claim 54, wherein the liquid medium is a supporting medium.

- 77. (Previously presented) The method of claim 76, wherein the supporting medium is a biocompatible solution having an osmotic activity of a monovalent electrolyte with concentration in the range between 1 mM and 500 mM.
- 78. (Previously presented) The method of claim 76, wherein the supporting medium is a biocompatible solution having an osmotic activity of a monovalent electrolyte with concentration in the range between 10 mM and 400 mM.
- 79. (Previously presented) The method of claim 76, wherein the supporting medium is a biocompatible solution having an osmotic activity of a monovalent electrolyte with concentration in the range between 50 mM and 300 mM.
- 80. (Previously presented) The method of claim 76, wherein the supporting medium is a biocompatible solution having an osmotic activity of a monovalent electrolyte with concentration in the range between 100 mM and 200 mM.
- 81. (Currently amended) The method of claim 76, wherein the supporting medium is a biocompatible solution that has practically sufficient penetrant stability combined with practically sufficient transport rate across a barrier.
- 82. (Previously presented) The method of claim 76, wherein the supporting medium is a biocompatible buffer with pH of between 4 and 10.
- 83. (Currently amended) The method of claim 54, wherein the <u>active ingredient</u> relative drug or agent concentration is between 0.001 and 40 weight-% of total penetrant mass.
- 84. (Currently amended) The method of claim 54, wherein the <u>active ingredient</u> relative drug or agent concentration is between 0.01 w-% and 30 w-% of total penetrant mass.
- 85. (Currently amended) The method of claim 54, wherein the <u>active ingredient</u> relative drug or agent concentration is between 0.1 w-% and 25 w-% of total penetrant mass.

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- 86. (Currently amended) The method of claim 54, wherein the <u>active ingredient</u> relative drug or agent concentration is between 0.5 w-% and 15 w-% of total penetrant mass.
- 87. (Previously presented) The method of claim 54, wherein the applied penetrant dose is between 0.01 mg and 15 mg per nostril.
- 88. (Previously presented) The method of claim 54, wherein the pharmaceutical formulation is administered using a metered delivery device.
- 89. (Previously presented) The method of claim 54, wherein the penetrants are in suspension and further comprising loading the penetrants with the active ingredient within 24 hours prior to the formulation administration before transnasal administration.
- 90. (Previously presented) The method of claim 54, wherein a target site of the active ingredient is a nervous system.
- 91. (Previously presented) The method of claim 90 wherein the target site is a brain.
- 92. (Previously presented) The method of claim 54, wherein the pharmaceutical composition is a vaccine.
- 93. (Previously presented) The method of claim 92, wherein the vaccine further comprises a pathogen extract or a compound from a pathogen or a fragment or a derivative thereof.
- 94. (Previously presented) The method of claim 92, wherein the vaccine further comprises an adjuvant.
- 95. (Previously presented) The method of claim 94, wherein the adjuvant is lipopolysaccharide, or an extract of a microorganism.
- 96. (Previously presented) The method of claim 92, wherein the vaccine comprises MPL and IL-12 or GM-CSF and IL-4.
- 97. (Currently amended) The method of claim 92, wherein at least one two doses of vaccine is are administered.

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98. (Previously presented) The method of claim 92, wherein the vaccine is administered as a booster vaccination.

- 99. (Previously presented) The method of claim 92, wherein the time interval between the subsequent vaccinations is between 2 weeks and 5 years.
- 100. (Currently amended) A method for administering a pharmaceutical composition to a patient in need thereof, comprising:

transnasally administering to the patient a pharmaceutical composition,

wherein the pharmaceutical composition is for the treatment of infective diseases, endocrine disorders, adrenal disorders, gastrointestinal disorders, hemorrhagic diseases, musculoskeletal and connective tissue disorders, neurological disorders, oncological disorders, psychiatric disorders, and/or for use in the field of gynecology, and/or for use in the field of immunology,

the pharmaceutical composition comprising:

an active ingredient; and

a carrier comprising a penetrant suspended or dispersed in a solvent,

the penetrant comprising a minute fluid droplet surrounded by a coating of at least one layer of at least two substances, the substances differing by at least a factor of 10 in solubility in a liquid medium,

the substances forming homoaggregates of one substance and/or heteroaggregates of the at least two substances, the average diameter of homoaggregates of the more soluble substance or the average diameter of the heteroaggregates of the at least two substances being smaller than the average diameter of homoaggregates of the less soluble substance, and/or

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the more soluble substance solubilizing the droplet and the content of the more soluble substance is up to 99 mol-% of the concentration required to solubilize the droplet or corresponds to up to 99 mol-% of the saturating concentration in an unsolubilized droplet, whichever is higher, and/or

wherein the elastic deformation energy of the droplet surrounded by the coating is at least five times lower than the deformation energy of red blood cells or of a phospholipid bilayer having fluid aliphatic chains.

- 101. (Previously presented) The method of claim 100, wherein the active ingredient is an antigen.
- 102. (Previously presented) The method of claim 101, wherein the antigen is derived from a pathogen.
- 103. (Previously presented) The method of claim 100, wherein the active ingredient is an allergen.
- 104. (Currently amended) A pharmaceutical composition for transnasal administration comprising:

an active ingredient; and

a transnasal carrier comprising a penetrant suspended or dispersed in a solvent,

the penetrant comprising a minute fluid droplet surrounded by a coating of at least one layer of at least two substances, the substances differing by at least a factor of 10 in solubility in a liquid medium,

the substances forming homoaggregates of one substance and/or heteroaggregates of the at least two substances, the average diameter of homoaggregates of the more soluble substance or the average diameter of the heteroaggregates of the at

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least two substances being smaller than the average diameter of homoaggregates of the less soluble substance, and/or

the more soluble substance solubilizing the droplet and the content of the more soluble substance is up to 99 mol-% of the concentration required to solubilize the droplet or corresponds to up to 99 mol-% of the saturating concentration in an unsolubilized droplet, whichever is higher, and/or

wherein the elastic deformation energy of the droplet surrounded by the coating is at least five times lower than the deformation of red blood cells or of a phospholipid bilayer having fluid aliphatic chains.